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Primary Hepatic Non-Hodgkin's Lymphoma in Children: A Case Report and Review of the Literature

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Non-Hodgkin's lymphomas presenting exclusively in the liver are rather uncommon in adults and extremely rare in children. We describe a six-year-old white boy with jaundice, abdominal pain, and weight loss of two weeks duration. Physical examination disclosed asthenia, jaundice, abdominal swelling, large hepatomegaly, and ascitis. Aminotransferases, bilirubin, and alkaline phosphatase were significantly elevated. Bone marrow aspiration, cerebrospinal fluid, chest x-ray, renal function tests, and uric acid were normal. Abdominal ultrasound showed liver enlargement with irregular borders, many parenchymal nodules in both liver lobes, a large hypoechogenic mass in the inferior segment of the liver, normal biliary ducts and two pancreatic nodules resembling those in the liver. Liver needle biopsy disclosed diffuse lymphomatous infiltration. Blast cells were positive for leukocyte common antigen (CD 45). Immunohistochemistry study for T or B cell lineage differentiation was not done. The child showed an excellent response to chemotherapy based on the BFM-83 protocol for B cell non-Hodgkin's lymphomas. The patient had his therapy discontinued in June 1995 and remains in first complete remission as of May 20th, 1996. Med. Pediatr. Oncol. 28:370–372, 1997. © 1997 Wiley-Liss, Inc.

INTRODUCTION

Lymphomatous involvement of the liver is rather common in non-Hodgkin's lymphomas, but primary exclusively hepatic presentation of lymphoma is extremely unusual at any age [1,2,3]. Three children with lymphoma restricted to the liver [4,5,6], a fourth child with a hepatic lymphoma and also a pancreatic lymphomatous nodule [5] and a fifth case with hepatosplenic lymphoma [5] have been described. We report an additional case of a male white child with primary hepatic non-Hodgkin's lymphoma along with two pancreatic nodules.

CASE REPORT

A six-year-old white boy was admitted at the Hospital of Clinics, Federal University of Minas Gerais in April 1994. He was asymptomatic until 15 days before admission when he developed progressive jaundice, dark urine, clay-colored stools, abdominal pain, nausea, and vomiting. During this period there was no fever. Physical examination disclosed weight loss (about 3 kg in two weeks), jaundice, abdominal tenderness and swelling (68 cm in diameter), hepatomegaly 9 cm from the right costal margin, and no palpable spleen. Small cervical and submandibular lymphnodes were not clinically significant and thus were not biopsied.

Complete blood count, chest x-ray, renal tests, urinalysis, serum electrolytes, partial thromboplastin, and prothrombin times, protein electrophoresis were normal. Cytocentrifugal cerebrospinal fluid examination did not show any blast cells. Bone marrow cell count registered 0.2% blast cells. Trephine marrow biopsy was not done. Total bilirubin was 13.5 mg/dl (10.6 mg/dl direct); serum aspartate aminotransferase 242 IU/L and alanine aminotransferase 150 IU/L; alkaline phosphatase 2400 IU/L (normal, 74 to 397); gamma-glutammyl transferase 76 IU/L (normal, 5 to 55), and lactate dehydrogenase 2947 IU/L. Serologic markers for A, B, and C hepatitis were negative. Serum α-fetoprotein concentration and urinary vanillylmandelic acid excretion were both normal.

Abdominal ultrasound showed that the liver was extremely enlarged, with numerous solid hypoechogenic nodules, some of them confluent and well delineated in relation to the parenchyma, distributed in both right and left lobes. From the right inferior hepatic border emerged a 11.9 × 8.7 × 10 cm mass with the same characteristics and no evidence of calcification or necrosis. Intrahepatic biliary ducts were slightly enlarged. The common bile duct and gall bladder were normal. The pancreatic head

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TABLE 1. Clinical Data, Laboratory Findings, and Outcome of Six Children With Primary Hepatic Non-Hodgkin's Lymphoma

Case (ref)	Age (y)/ Sex	Initial Symptoms	Physical Examination	Gross Liver Disease/ Extrahepatic Involvement	Histology/ Surface Markers	Therapy[a]	Survival (Months)	Outcome
1 (5)	8/M	abdominal pain	Enlarged liver (6 cm), no lymphnodes, normal spleen	Coalescent nodules in the left lobe/none	Diffuse undifferentiated NHL/not done	CTX and irradiation	5½	Died; widely metastatic disease
2 (5)	7/M	abdominal pain	Enlarged (? cm) liver and spleen. No lymphnodes	12 cm mass in the left lobe/1.5 cm pancreatic nodule	Poorly differentiated lymphocytic lymphoma/B cell	CTX, VCR, MTX, DXR. LSA2L2 + irradiation	7	Died; persistent liver enlargement; bone marrow and CNS disease
3 (5)	13/M	fatigue, abdominal swelling	Enlarged liver (9 cm) and palpable spleen (10 cm)	multiple large nodules/ spleen nodules	Diffuse hystiocytic lymphoma/B cell	Splenectomy + LSA2L2 + irradiation	22 (+)	Clinical remission
4 (6)	11/M	abdominal swelling	Hepatomegaly (? cm)	large right lobe mass/none	Unclassifiable NHL/[b]LCA+, B−, T−	Hepatic right lobectomy + DXR	30 (+)	Clinical remission
5 (4)	12/M	fever, jaundice, abdominal mass	jaundice, enlarged liver (5 cm), cervical lymphnodes mildly enlarged	large intrahepatic mass/none	Diffuse large cell lymphoma/ B cell. Near-tetraploid karyotype; t(8;14)	High dose MTX, CTX, VCR, PDN, VP-16, ARA-C and DXR	10 (+)	Clinical remission
6 (Present case)	6/M	jaundice, abdominal pain	jaundice, palpable liver (9 cm), normal spleen, no lymphnodes	multiple nodules/two pancreatic nodules (4.2 × 3.1 cm and 1.8 × 1.8 cm)	Diffuse small noncleaved cell lymphoma/ CD45+, B and T not done	BFM-83 for B cell NHL	25 (+)	Clinical remission

[a] CTX, cyclophosphamide; VCR, vincristine; MTX, methotrexate; DXR, doxorubicin; ARA-C, cytosine-arabinoside; VP-16, etoposide; PDN, prednisone, LSA2L2, Sloan-Kettering protocol for non-Hodgkin's lymphoma.
[b] LCA, leukocyte common antigen.

had normal characteristics; the body and tail showed two rounded hypoechogenic nodules, well delineated, measuring respectively 4.2 × 3.1 cm and 1.8 × 1.8 cm. The splenic vein was posteriorly displaced. The hepatic hylar region was extremely difficult to visualize due to abundant nodes deforming the organ shape in this region; only a small ovoid lymphnode measuring 1.3 × 0.7 cm was observed. The kidneys, spleen, aorta, and inferior cava vein were unremarkable.

A computerized tomography scan showed that the liver was extremely enlarged and had a heterogenic texture and lobulated rims; small segmented dilatations of the biliary ducts were also seen. The gallbladder, kidneys, and spleen were normal. The pancreas was not well seen.

An ultrasound-guided needle biopsy of the liver showed diffuse infiltration by tumoral lymphocytic small cells (diffuse small noncleaved cell lymphoma, NCI working formulation). Leukocyte common antigen (CD45) was detected by monoclonal antibody in the blast cells infiltrating the liver parenchyma. T or B lineage differentiation could not be performed.

The BFM-83 chemotherapeutic protocol for non-Hodgkin's B cell lymphomas [7] was started on May 5th, 1994. The child showed remarkable clinical improvement during the first week of treatment and hepatomegaly significantly decreased after three weeks. Complete clinical remission, defined by the complete disappearance of a palpable liver, occurred in October 1994. Therapy was discontinued in June 1995. The patient remains in first complete remission as of May 20th, 1996.

DISCUSSION

Primary lymphoma of the liver is extremely uncommon in adults and exceptionally rare in childhood. Os-

borne et al described 19 cases up to 1980 [8]. Anthony et al described 10 cases from 1980–1990 [9]. Scoazec et al [10] and Shibata et al [11] described in 1991 eight and one cases, respectively, and Pereira et al [12] described two further cases in 1993, all adult patients.

Miller et al described in 1983 the first 3 childhood cases [5], followed by Mills [6] in 1988 and Collins et al [4] in 1993 with one case each. The table summarizes these cases and the present one. Our case illustrates the typical clinical features already described in the literature: jaundice, abdominal pain, and hepatomegaly. It is noteworthy that all were male up to now. Although cell lineage differentiation was not available because biopsy specimen was too small, the clinical presentation and B cell predominance described in the literature prompted us to choose B-cell directed chemotherapy. Out of five pediatric cases, three had B-cell differentiation [4,5] and in two immunophenotyping was inconclusive [6] or was not done [5].

The excellent response to chemotherapy and definite chance of cure emphasize considering primary lymphoma of the liver as part of the differential diagnosis of primary liver tumor in children, mainly in the presence of normal serum fetoprotein levels. Other possible histologic diagnoses are embryonal sarcoma of the liver, metastatic neuroblastoma, rhabdomyosarcoma, Ewing's sarcoma, and some types of Wilms' tumor.

Chemotherapy alone was able to induce and maintain remission now for two years in the present case, as also reported by Collins et al [4]. We feel that children with primary hepatic lymphoma should have a chance to be treated with multiagent chemotherapy alone, avoiding extensive hepatic lobectomy. Such recommendation is similar to that for advanced childhood non-Hodgkin's lymphomas of other sites in which radical surgical removal of the tumor may needlessly mutilate the child. The key to this clinical approach is to be sure about the histologic diagnosis which is indeed very difficult to establish without confirmatory immunophenotyping.

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